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EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	
ART UNIT	**PAPER NUMBER**
1648	

MAIL DATE	DELIVERY MODE
11/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/686,943	MCMICHAEL ET AL.	
	Examiner	Art Unit	
	Louise Humphrey, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *8,9,11,13,17-26,29-31,34 and 35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,7,10,12,14-16,27,28,32 and 33* is/are rejected.

7)☒ Claim(s) *5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/6/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the amendment filed 06 September 2007. Claims 1-35 are pending. Claims 8, 9, 11, 13, 17-26, 29, 30, 31, 34 and 35 are withdrawn. Claim 31 is now withdrawn in response to Applicants' amendment deleting the elected invention of SEQ ID NO:64. Claims 1-7, 10, 12, 14-16, 27, 28, 32 and 33 are pending and currently examined.

Claim Objections

Claim 5 is objected to because it is drawn in part to nonelected inventions and it depends from a rejected claim. Appropriate correction is required.

Affidavit under 37 CFR 1.132

The Mackett declaration under 37 CFR 1.132 filed on 06 September 2007 is insufficient to overcome the rejection of claims 1-4, 6, 7, 10, 12, 14-16, 27, 28, 32 and 33 based upon the Li reference (1993), Sutter reference (1992) and Stoute reference (1997) as set forth in the last Office action because the affidavit fails to set forth any facts. It includes statements which amount to an affirmation that the affiant has never seen the claimed subject matter before. This is not relevant to the issue of nonobviousness of the claimed subject matter and provides no objective evidence thereof. See MPEP § 716. Dr. Mackett's opinion that a non-replicating or replication-impaired virus is not expected to be effective is not germane to the rejection at issue.

In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence of nonobviousness fails to outweigh the evidence of obviousness.

Double Patenting

The nonstatutory double patenting rejection of claims 1-6, 10, 14-16, 27 and 31-33 as being unpatentable over claims 1, 2, 5-7, 15-18, and 20 of U.S. Patent No. 6,663,871 will be withdrawn upon Applicants' submission of a compliant terminal disclaimer. The statutory rejection under 35 U.S.C. §101 of claims 45-52 and 56-61 as claiming the same invention as that of claims 35, 37-45 and 48-51 of US Patent No. 6,737,066 B1 is maintained until Applicant cancels or amends the conflicting claims so they are no longer coextensive in scope.

The provisional nonstatutory double patenting rejection of claims 1-3, 6, 7, 10, 12, 14 and 15 as being unpatentable over claims 1,4, 5, 9, 11, 13 and 14 of copending Application No. 10/833,439, of claims 1-3, 6, 7, 10,. 12, 14 and 15 as being unpatentable over claims 1,4, 5, 9, 11 and 13-16 of copending Application No. 10/833,744, of claims 1-3, 5-7, 10, 12, 14 and 15 as being unpatentable over claims 1,4, 5, 9, 11, and 13-15 of copending Application No. 10/833,745, and of claims 1, 6 and 27 as being unpatentable over claims 1-5 and 6-8 of copending Application No. 10/653,624 are held in abeyance until allowable subject matter is determined.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 1-3, 6, 10, 12, 14 and 15 under 35 U.S.C. §103(a) as being obvious over Pialoux *et al.* (1995) in view of Egan *et al.* (1995) is **withdrawn** in consideration of Applicants' arguments regarding the unpredictability of reverse the order of the prime-boost regime.

The rejection of claims 1-3, 5, 6, 10, 12, 14 and 15 under 35 U.S.C. §103(a) as being obvious over Pialoux *et al.* (1995) in view of Egan *et al.* (1995), and further in view of Walker *et al.* (1989) is **withdrawn** for the same reason as set forth above.

The rejection of claims 1-4, 6, 7, 10, 12, 14-16, 27, 28, 32 and 33 under 35 U.S.C. §103(a) as being unpatentable over Li *et al.* (1993, reference No. AU4 in IDS filed on 06 July 2004) in view of Sutter *et al.* (1992, reference No. C52 in IDS filed on 09 November 2006) and Stoute *et al.* (1997, January) is **maintained**.

Li *et al.* describe priming with recombinant influenza virus followed by boosting with recombinant vaccinia virus induces $CD8^+$ T-cell-mediated protective immunity against malaria. The sequence of immunization appears to be crucial, since a primer injection with recombinant vaccinia virus, followed by a booster injection with recombinant influenza virus, failed to induce protection. The protection induced by immunization with these recombinant viruses is mostly mediated by CD8+ T cells. See

abstract. Suggested routes of administration were i.p., by aerosol, and intravenous injection. See p. 5215, left column.

Li *et al.* do not describe a replication-impaired or non-replicating recombinant virus vector in the boosting composition and an adjuvant.

Sutter *et al.* describe a non-replicating vaccinia vector, modified vaccinia Ankara (MVA) strain that has been safety tested in humans. See Abstract.

Stoute *et al.* describe malaria vaccine formulations in three kinds of adjuvants: alum and monophosphoryl lipid A (SBAS4), an oil-in-water emulsion (SBAS3), and an oil-in-water emulsion plus the immune stimulants monophosphoryl lipid A and QS21 (SBAS2). The vaccines were administered intramuscularly. See p. 87, Study Design and Vaccines. Stoute *et al.* further describe that SBAS2 is the most efficacious adjuvant. See p. 90, Discussion.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the prime-boost method of Li *et al.* by replacing the boosting recombinant vaccinia virus with a safer non-replicating vaccinia virus, the MVA, as taught by Sutter *et al.* One having ordinary skill in the art would have been motivated to do this because a live vaccinia virus is infectious while MVA does not replicate in mammalian cells yet expresses recombinant genes efficiently, as suggested by Sutter *et al.* It also would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the prime-boost method of Li *et al.* by adding the SBAS2 adjuvant as taught by Stoute *et al.* One having ordinary skill in the art would have been motivated to do this because SBAS2 may also provide signals required to

up-regulate co-stimulatory molecules on antigen-presenting cells, induce expression of molecules that permit these cells to travel to target tissues, or induce production of cytokines that mediate protection, as per suggested by Stoute *et al.* There would have been a reasonable expectation of success, given the results that the SBAS2 formulation proved superior for inducing strong antibody responses and strong antigen-specific delayed hypersensitivity in primates and proliferative and cytolytic T cell responses in mice, as taught by Stoute *et al.* Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Applicants argue that the " synergistic effect" achieved through Li's method of using a recombinant influenza virus prime and replicating recombinant vaccinia virus boost clearly teaches away from modifying their successful immunization method. Applicants further argue that Sutter *et al.* do not teach that their MVA vector can elicit a $CD8^+$ T cell response in a mammal and point to the uncertainty of using MVA in immunization methods in mammals by teaching that "[w]hether MVA vectors will also be useful for live vaccine or therapeutic applications remains to be determined."

Applicants' argument regarding the particular order of priming with an influenza virus and boosting with a recombinant vaccinia virus (rVV) is not germane to the rejection at issue. The examiner never suggested reversing the order of injection of the priming influenza virus and the boosting rVV in this rejection. On the contrary, the Lu *et al.* reference was proffered to meet the limitation of boosting with a recombinant virus vector and the limitation of using different viruses in the priming and boosting

compositions. The mere "synergistic effect" does not prevent one skilled in the art from modifying Li's immunization method for improved safety in human.

The Sutter *et al.* reference was offered for teaching the claimed non-replicating or replication-impaired virus vector. Even though Sutter *et al.* are silent on the type of immune response elicited by MVA, Sutter *et al.* clearly provides the motivation for one skilled in the art to substitute a recombinant vaccinia virus with the replication-impaired vaccinia virus, MVA, because of its safety in mammals yet high efficiency in expressing foreign proteins in human cells (page 10847). The statement "[w]hether MVA vectors will also be useful for live vaccine or therapeutic applications remains to be determined" does not deny the feasibility of MVA vectors as a vehicle for delivery of immunogens but actually motivates a skilled artisan to investigate the effectiveness of MVA vectors in immunization methods.

Applicants' assertion that the opinion of those of skill in the art, including Dr. Mackett's declaration, is that an immune response requires a replication-competent virus is not germane to the rejection at issue. The opinion does not set forth any facts purporting to be objective evidence.

Thus, the combination of Sutter *et al.* and Li *et al.* is properly motivated and a *prima facie* case of obviousness is properly established.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached at 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Jeffrey Parkin, Ph.D.
Primary Examiner
01 November 2007

Louise Humphrey, Ph.D.
Assistant Examiner